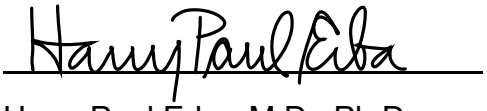
Expert Report of Harry Paul Erba, M.D., Ph.D.

Vivian Connard, Representative of
Stephen Matthew Connard, deceased v. United States
7:23-cv-01557-D-RN
U.S. District Court for the Eastern District of North Carolina

Prepared By:



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their metabolites. If these foreign substances do reach the bone marrow, HSC have at least two mechanisms that protect against DNA damage. HSC express drug efflux pumps such as P-glycoprotein on their cell surface that can eliminate harmful chemicals from reaching the DNA in the HSC nucleus. Furthermore, there are DNA repair enzymes that can fix damage caused by chemicals such as alkylating agents. Therefore, like ionizing radiation, there is a threshold amount of exposure to DNA damaging chemicals that is required to overcome these protective mechanisms and cause DNA damage followed by either cellular apoptosis or leukemic transformation.

Secondary AML (not de novo, or idiopathic) is associated with exposure to cytotoxic chemotherapy, ionizing radiation, and environmental toxins. AML cases due to DNA-damaging chemotherapy agents (such as alkylating agents) typically occur within 10 years of exposure. The risk of AML following such exposure has been directly associated with the dose as well (for example, see Curtis RE, et al. N Engl J Med. 1992; 326: 1745-51; Jonsdottir G, et al. Eur. J. Haematol. 2021; 107: 275-282). Secondary AML cases often have adverse cytogenetic features like monosomy 7 and are refractory to chemotherapy. However, these clinical and pathologic findings are not specific for therapy-related AML (tAML). In the Danish registry study, 40% of therapy-related AML patients had adverse risk karyotypes (like monosomy 7) but so did 18% of de novo AML patients (Granfeldt-Ostgard LS, et al. J Clin Oncol. 2015; 33: 3641).

As Dr. Goodman explains in her general causation report, there is little data to support a causal connection between leukemia and TCE or PCE. In the analysis of the New Jersey drinking water contamination, there was no increased risk of AML at any TCE exposure level (Cohn P, et al. Environ Health Perspectives 1994; 102: 556-561). The same is true for all leukemia subtypes and PCE exposure.

Dr. Goodman agrees that benzene can cause AML, but she concludes that sufficient exposures are required. The details of the high-quality Chinese workers study and the Pliofilm study discussed in Dr. Goodman's report are critical to understand in relation to Mr. Connard's AML. In those studies, a statistically significant increase in AML was demonstrated in workers who were exposed to at least 40-75 ppm-years of cumulative benzene exposure, and the latency between exposure and development of leukemia was generally within 10 years (see Dr. Goodman's 02/07/2025 report at 87-88).

In Mr. Connard's case, he was at Camp Lejeune for less than three years, and, as Dr. Bailey estimates in her risk assessment report, his cumulative exposure to benzene was at most 0.00033 ppm-years, which is orders of magnitude below the thresholds of 40-75 ppm-years indicated in the Chinese workers and Pliofilm studies. As Dr. Bailey explains, Mr. Connard's estimated lifetime increase of risk was 0.0001%, which is equivalent to 1 in 1,000,000 exposed people. Given the annual incidence of AML in the year 2000 was 3.9 cases per 100,000, Mr. Connard's increased AML risk was significantly below the expected.

Regarding latency, Mr. Connard developed AML just shy of 20 years (19.75, to be exact) after leaving Camp Lejeune, which is nearly twice the ten-year latency periods demonstrated in the Chinese workers and Pliofilm studies. Although it is conceivable that Mr. Connard could have had an undiagnosed myelodysplastic syndrome prior to progression to AML, documentation of his